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Association between psychosocial work-related factors at midlife and arterial stiffness at older age among 1,736 white-collar workers

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Abstract

Objective – Arterial stiffness and exposure to psychosocial work-related factors increase the risk of developing cardiovascular disease (CVD). However, little is known about the relationship between psychosocial work-related factors and arterial stiffness. We aimed to examine this relationship.

Methods – The sample included 1,736 (female 52%) participants from the PROspective Québec Study on Work and Health, a three-wave cohort study (T1:1991-1993, T2:1999-2001 and T3: 2015-2018) of white-collar workers in Quebec City (Canada). Psychosocial work-related factors, job strain and effort-reward imbalance (ERI), were assessed at T2 with validated instruments. Arterial stiffness was assessed using carotid-femoral pulse wave velocity at T3, on average 16 years later. Generalized estimating equations were used to estimate differences in arterial stiffness between exposed and unexposed participants. Subgroup analyses according to sex, age, blood pressure (BP), cardiovascular risk score and employment status were conducted.

Results – Among participants with high diastolic BP (≥90 mmHg) at T2, aged 47 on average, those exposed to high job strain had higher arterial stiffness (+1.38 m/s (95% CI: +0.57; +2.19)) at T3, 16 years later, following adjustment for a large set of potential confounders. The trend was similar in participants with high systolic BP (≥140 mmHg) exposed to high job strain (+0.84 m/s (95% CI: -0.35; +2.03)). No association was observed for ERI in the total sample and counterintuitive associations were observed in subgroup analyses.

Conclusions –Job strain may have a long-term deleterious effect on arterial stiffness in people with high BP. Interventions at midlife to reduce job strain may mitigate arterial stiffness progression.

Strengths and limitations of this study

- This study has a long follow-up period of 16 years.
- Arterial stiffness was measured using carotid-femoral pulse wave velocity, the gold standard.
- Psychosocial work-related factors were assessed using validated tools.
- This study examines the effect of psychosocial work-related factors measured at a single point in time.

Key questions

What is already known on this subject?

There is evidence that adverse psychosocial work-related factors contribute to the development of cardiovascular disease. Arterial stiffness, measured using carotid-femoral pulse wave velocity (cfPWV), is a major predictor of cardiovascular mortality and morbidity. Little is known about the relationship between psychosocial work-related factors and arterial stiffness.

What might this study add?

The present longitudinal study including 1,736 white-collar workers examined the long-term effects of exposure to psychosocial work-related factors (job strain and effort-reward imbalance) on arterial stiffness measured using cfPWV (gold standard). The study suggests that participants with high BP who are exposed to job strain at midlife (mean age < 50 years) may have increased arterial stiffness 16 years later.

How might this impact on clinical practice?

Because psychosocial work-related factors from the job strain model are frequent and modifiable, interventions to reduce exposure to these risk factors early on may mitigate arterial stiffness progression.

Introduction

Cardiovascular disease (CVD) is a major public health problem. CVD develops over several years across a continuum initiated by one or several risk factors, which can progress to atherosclerosis, cardiovascular events and end-stage organ disease (1). The main modifiable risk factors for CVD include dyslipidemia, high blood pressure (BP), smoking, diabetes and adiposity. Additional factors such as psychosocial work-related factors can contribute to increase the risk of CVD (2). In Organisation for Economic Co-operation and Development countries, 20-25% of workers are exposed to adverse psychosocial work-related factors (3).

Arterial stiffness describes the reduced ability of large proximal arteries to dilate and retract. Carotid-femoral pulse wave velocity (cfPWV), the gold standard method for assessing aortic stiffness, is linearly associated with CVD risk (4). An increase in aortic pulse wave velocity of 1 m/s corresponds to an adjusted risk increase of 14% in fatal or nonfatal cardiovascular events (4). Adverse psychosocial work-related factors may be associated with high arterial stiffness. Results of prior studies differ according to types of exposure and sex, suggesting deleterious (5-9), beneficial (10) or no effect (11) of psychosocial work-related factors on arterial stiffness. All prior studies are limited by their cross-sectional design. None used the gold standard measure for arterial stiffness.

The objective of the present study was to examine the association between psychosocial work-related factors and arterial stiffness in a prospective cohort study of men and women from Quebec City, Canada. Men and women were considered separately since the prevalence of psychosocial work-related factors and their effects differ by sex (2). Elevated midlife BP is associated with increased arterial stiffness (12). The relationship between midlife psychosocial work-related factors and arterial stiffness might therefore vary between people with and without elevated BP. This potential effect modification was examined.

Methods

Population and study design

Data were drawn from a three-wave (T1:1991-1993, T2:1999-2001 and T3: 2015-2018) prospective cohort study including, at T1, 9,188 white-collar workers (participation proportion: 75%) from 19 public organizations in Quebec City, aged 18 to 65 years old. Among participants at T1, 8,120 (88.4 %) and 6,707 (73 %) participated at T2 and T3, respectively. Arterial stiffness was measured in 1/3 of participants randomly selected. The final sample included 1,736 participants with employee status at T2 (Figure 1). The *Centre Hospitalier Universitaire de Québec – Université Laval* (CHUdeQc-UL) ethical research committee (2012-1674; DR-002-1409; F9H-63202) approved the study. All participants signed an informed consent form.

Data collection

At each wave, workers completed a self-administered questionnaire on risk factors for hypertension and CVD, demographic, occupational and social characteristics. Trained staff measured BP (using the mercury sphygmomanometer at T1 and T2 and the automated BP-TRU device (VSM MedTech, Coquitlam, Canada) at T3), height, weight, and waist circumference. Arterial stiffness was measured at T3.

Psychosocial work-related factors

Job strain and effort-reward imbalance (ERI) exposures were assessed at T2 (1999-2001). Components of job strain (psychological demands and job control) were measured using 18 items from the Job Content Questionnaire (13). Psychological demands include the quantity of work, time constraints and level of intellectual effort. Job control includes opportunities for learning, autonomy, and participation in the decision-making process. The theoretical model postulates that the greatest health risk occurs in workers combining high demands and low control. The psychometric properties of the original English (14) and French (15) questionnaires have been demonstrated. We classified workers with demands scores≥24 (the median in the Quebec working population) in the *high demands* group and those with control scores≤72 (the median in the Quebec working population) in the *low control* group. The *low strain* group included workers combining *low demands* and *high control*. The p*assive*, *active* and *high strain* groups included respectively people combining *low demands* and *low control*, *high demands* and *high control* and *high demands* and *low control*.

The ERI model states that efforts should be rewarded with income, respect and esteem, and occupational status control. Workers are in a state of deleterious imbalance when high efforts are accompanied by low reward, and are more susceptible to health problems. The modified French version of the questionnaire was used to assess ERI. Reward at work was measured by nine original questions from the French version (16) of the ERI scale. Effort was measured by nine items from the validated French version of the psychological demand scale of the Job Content Questionnaire (17). The psychometric qualities of this ERI scale version have been demonstrated (18). Effort and reward scores were computed with the sum of items. A ratio efforts/reward>1 indicated an imbalance. The ratio was also used in its continuous form.

Arterial stiffness as cfPWV (m/s)

Arterial stiffness was measured at T3 using the Complior Analyse device (Alam Medical, Saint-Quentin-Fallavier, France). The transit time between the carotid and the femoral pulse was measured twice in each participant. cfPWV was calculated by dividing the carotid-femoral transit distance (calculated using the difference in body surface measurements from the suprasternal notch to the femoral and carotid sites) by the carotid-femoral transit time delay. A third measurement was taken if the difference between the two measurements was >0.5 m/s. Inter- and intra-observer reproducibility of this measurement has been reported as excellent (19).

Covariates

Potential confounders included the following risk factors for arterial stiffness: demographic characteristics (age, sex, education, household income, marital status and having children); biological factors (BP, body mass index (BMI), waist circumference, diabetes, hypercholesterolemia and personal history of cardiovascular event), lifestyle factors (daily smoking, alcohol abuse and leisure time physical activity); family history of CVD at ≤ 60 years of age; psychological distress (Psychiatric Symptom Index); other work factors (hours worked for the organization, hours worked for another organization).

Statistical analyses

Continuous data were expressed as the mean along with the standard deviation. Categorical data were expressed as number and percentages. Generalized estimating equations were used to estimate differences in arterial stiffness means between the exposed and unexposed groups, with their 95% confidence interval (20). Regression models accounted for the correlation between employees of the same organization. The models were sequentially adjusted for sets of covariates given that biological factors, psychological distress and lifestyle factors potentially mediate the associations (Figure S1, supplement). As job strain and ERI models provide distinct information, we assessed the independent effect of job strain and ERI by adjusting for job strain when measuring the association with ERI and vice versa. In order to assess effect modification, we conducted subgroup analyzes by sex and BP (systolic, diastolic and pulse pressure) at T2. Sensitivity analyses were also conducted i) with and without individuals with personal history of CVD since they may have increased arterial stiffness; ii) according to risk factors for arterial stiffness at T2 (age and Gaziano's cardiovascular risk score (21)) since they may increase the deleterious effects of psychosocial work-related factors (22); iii) according to job status at T3 since retirement may attenuate the effects of psychosocial work-related factors (23). Multiple imputations and inverse probability weighting were performed to minimize potential selection bias due to non-response and/or loss to follow-up. Analyses were performed with SAS 9.4 software. The level of statistical significance was set at 0.05.

Participant and public involvement

Patients or the public were not involved in the study design, conduct, reporting, or dissemination plans.

Results

Mean follow-up time between exposure (T2) and arterial stiffness assessment (T3) was 16.8 (standard deviation: 1.3) years. At T2, participants were on average 45 years old. More women (23%) than men (17%) were exposed to high job strain. As many men as women were exposed to ERI (24%). At T3, participants were on average 62 years old (Table 1).

Table 2 presents mean arterial stiffness at T3 in men and women according to main risk factors for cardiovascular diseases and psychosocial work-related factor at T2. Arterial stiffness (mean:8.1± 1.7 m/s) was higher in men, in older participants and among those with high BP, diabetes, hypercholesterolemia, high waist circumference, high BMI and moderate or high cardiovascular risk score.

Table 3 presents the association between psychosocial work-related factors at T2 and arterial stiffness at T3. In men, arterial stiffness was slightly higher in those with passive jobs. In women, arterial stiffness was higher in participants exposed to ERI. All differences were modest and not statistically significant, with confidence intervals including the null value.

Table 4 presents the association between psychosocial work-related factors and arterial stiffness according to BP at T2. The high job strain group had higher arterial stiffness (+1.38 m/s (95%CI: +0.57; +2.19)) among participants with high diastolic BP (≥90 mmHg) and lower arterial stiffness (-0.25 (95%CI: -0.48;-0.02)) among those with lower diastolic BP (<90 mmHg). The same trend was observed for systolic BP. The high job strain group had higher arterial stiffness (+0.84 m/s (95% CI: -0.35; +2.03), p=0.17) among those with systolic BP≥140 mmHg. Arterial stiffness was also higher in the high job strain (+3.00 (95%CI:+1.18;+4.76)) and the passive (+2.06 (95%CI: +0.69;+3.44)) groups among participants with pulse pressure>60 mmHg. However, only 43 participants had high pulse pressure. ERI was associated with lower arterial stiffness in participants with systolic BP≥140 mmHg (-1.17 (95%CI:-2.12;-0.22)), in those with diastolic BP≥90 mmHg (-0.48 (95%CI:-1.10;+0.14)) and with pulse pressure>60 mmHg (-2.06 (95%CI:-3.33;-0.79)) (Table 4).

Supplementary analyses showed that arterial stiffness tended to be higher in participants exposed to job strain who were ≥55 years old or had a moderate or high CVD risk score. The ERI group had higher arterial stiffness in the 55+ age stratum (+0.52 (95%CI:-0.67;+1.71) (Table S1, supplement). Psychosocial work-related factors were not associated with arterial stiffness when stratifying according to employment status and duration of retirement (Table S2a and S2b, supplement). The findings were similar with and without participants with history of CVD (Table S3, supplement), and before and after multiple imputation and inverse probability weighting (Table S4, supplement).

Discussion

In the present study, arterial stiffness was not significantly higher in men and women exposed to high job strain and ERI overall. However, among participants with higher diastolic BP at midlife, high job strain was associated with higher arterial stiffness 16 years later. This association was robust to adjustment for socio-demographics, lifestyle-related risk factors, CVD risk factors and other factors from the work environment.

Prior studies assessing the relationship between psychosocial work-related factors and arterial stiffness were cross-sectional (5-11). Most suggest a deleterious effect (5-9). Studies suggesting a protective (10) or no effect (11) involved relatively young participants (≤40 years). Studies showing deleterious associations included people aged over 40 years on average (5-7, 9), a high proportion of smokers (>40%) (5, 6) or targeted workers in professions at higher risk of developing CVD such as firefighters (9). Given their cross-sectional design, previous studies do not inform on different aspects of the temporal relationship between psychosocial work-related factors and arterial stiffness, including the optimal time window and follow-up period. The time required between exposure to psychosocial work-related factors and arterial stiffness may vary according to the position of individuals on the cardiovascular continuum. A longer follow-up time could be required for participants who are at an earlier stage than for those who are at a more advanced stage of progression. In the present study, high job strain was associated with increased arterial stiffness 16 years later (+1.38 m/s), in participants with high diastolic BP at time of exposure assessment (T2). The mean age of participants with high DBP at T2 was 47 years old. Given that diastolic hypertension predominates in relatively young individuals, at a relatively early stage of the cardiovascular continuum and that CVD develops over at least a decade, it is reasonable to postulate that the follow-up period used in the present study was appropriate for measuring the association between midlife work-related factors and arterial stiffness in participants with high DBP at midlife (12, 24).

Increased arterial stiffness was also observed among participants with high systolic BP. This association was however of smaller magnitude and did not reach statistical significance. This is consistent with the natural history of systolic/diastolic BP progression and its links with CVD diseases onset (24). On the contrary, high job strain was associated with reduced arterial stiffness in participants who did not have high BP. Measuring the association between midlife stressors and arterial stiffness among people who do not have high BP may require a longer follow-up, which could explain the presence of this counterintuitive protective association. This is consistent with a previous cross-sectional study which showed a protective association between job strain index and brachial-ankle PWV (-1.38 m/s, p<0.01). This previous study included young participants (median age: 31 years) with diastolic (median: 79 mmHg) and systolic (median: 110 mmHg) BP in the normal range (10). Further studies are needed to confirm these results.

Due to limited statistical power, caution should be exercised in interpreting the trends of increased arterial stiffness among participants exposed to job strain in moderate to high cardiovascular risk score and older participants' strata. These results should be regarded as hypothesis generating. In our study, the participants who remained actively employed at T3 were relatively young (on average 39 years old) and had a low cardiovascular risk score (98%) when exposure was measured at T2. Younger age combined with low cardiovascular risk score may contribute to the absence of observed association. Indeed, among this younger subgroup, the timeframe for arterial stiffness assessment could have been suboptimal. ERI was associated with lower arterial stiffness in participants with high systolic BP, diastolic BP and high pulse pressure. This is counterintuitive and needs to be replicated.

In normotensive people without additional cardiovascular risk factors aged 60 to 69, the reference value for arterial stiffness is on average 10.3 m/s (25). In the present study, the average value (8.3 m/s) of participants in this age group (n=930) is lower. The attrition due to non-response and loss to follow-up may have contributed to these finding given the loss of individuals who may be sicker than those who participated, as demonstrated in this cohort (26). As expected, participants at higher risk of CVD (men, older age, high BP, diabetes, hypercholesterolemia, high waist circumference, high BMI, moderate or high cardiovascular risk score) generally had higher arterial stiffness than those at lower risk.

Chronic stress accelerates aging of arteries by incompletely understood mechanisms. Chronic stress can on one hand activate the sympathetic nervous system interconnected with the renin-angiotensin-aldosterone system and endothelin-1 activity and on the other hand promote risky lifestyle (27, 28). This leads to changes in vascular cell phenotypes and to thickening of the arterial innermost and intermediate layers, stiffness and increase in systolic and pulse pressure later on (27). Increased arterial stiffness causes excessive transmission of pulse pressure that can damage the microcirculation of target organs, which increases the risk of cardiovascular events (29). Older subjects or those with cardiovascular risk factors could have decreased endothelial regeneration capacity due to a reduced number of circulating progenitor endothelial cells (27, 30). A reduced regenerative capacity could explain a deleterious effect of job strain in people with an increased risk of developing a cardiovascular event given their age, cardiovascular risk score or high BP. Al Mheid et al. observed significant interactions ($P \leq 0.005$) between age and the burden of cardiovascular risk factors (smoking, diabetes mellitus, hypertension, or hyperlipidemia), such that for younger subjects (<40 years), cardiovascular risk factors were associated with increased progenitor cells counts, whereas for older subjects (>60 years), cardiovascular risk factors and CVD were associated with lower progenitor cells counts (30).

Our study has several strengths. To our knowledge, this is the first study to examine the association between psychosocial work-related factors assessed at midlife and arterial stiffness assessed at older age, using a prospective cohort. The 16-year follow-up allowed exploration of long-term effects. Other strengths are the use of a gold standard arterial stiffness measurement and validated psychosocial work-related factors models, sequential adjustment by several potentially confounding factors, inverse probability weighting to minimize the potential for selection bias and subgroup analyzes based on a priori evidence.

Our study has also limitations. First, the potential for selection bias due to a high proportion of missing values (40% out of 2,621 participants with employee status at T1 and T2) and losses to follow-up (19% out of 2,621) may underestimate associations (26). However, the associations were similar before and after accounting for potential selection bias using multiple imputations and inverse probability weighting, suggesting that this potential bias could not have explained our results. Second, the use of a single measure of exposure limits the capacity to capture fluctuations in exposure and can lead to non-differential misclassification of exposure that may underestimate the association. Third, measuring arterial stiffness in 1/3 of participants combined with attrition reduced statistical power. Fourth, the study population was entirely composed of white-collar workers. Caution is therefore advised in generalizing to other types of occupations.

Conclusion

Job strain exposure combined with high BP at midlife may have long-term deleterious effects on arterial stiffness. Interventions at midlife to reduce job strain may be considered as a potential way to manage CVD risk.

Acknowledgments and affiliations

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Contributors

VKM conceptualized and designed the study under the supervision of AM, DT and CB. VKM conducted the analysis and drafted the manuscript. All authors reviewed the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Table 1. Population characteristics at T2 (1999-2001) (unless otherwise stated) by sex

	Missing	All 1736 (100.0)%	Missing	Men 839 (48.3%)	Missing	Women 897 (51.7%)
Age y, mean (SD), T1 (1991-1993)	0	37.3 (6.6)	0	38.6 (6.9)		36.2 (6.1)
Age y, mean (SD), T2 (1999-2001)	0	44.9 (6.7)	0	46.2 (7.0)	0	43.8 (6.2)
Age y, mean (SD), T3 (2015-2018)	0	61.7 (6.1)	0	63.0 (6.4)		60.6 (5.6)
Job strain	16		7		9	
Low strain		298 (17.3)		174 (20.9)		124 (14.0)
Passive		592 (34.4)		237 (28.5)		355 (40.0)
Active		486 (28.3)		280 (33.7)		206 (23.2)
High strain		344 (20.0)		141 (17.0)		203 (22.9)
Effort-reward imbalance	47		24		23	
Yes		408 (24.2)		197 (24.2)		211 (24.1)
No		1281 (75.8)		618 (75.8)		663 (75.9)
Completed education	12		3		9	
Secondary or less		334 (19.4)		67 (8.0)		267 (30.1)
College (CEGEP)		530 (30.7)		238 (28.5)		292 (32.9)
University		860 (49.9)		531 (63.5)		329 (37.1)
Household income $C[a]	11		4		7	
0 - 49 999		426 (24.7)		144 (17.3)		282 (31.7)
50 000 - 79 999		681 (39.5)		362 (43.4)		319 (35.8)
≥ 80 000$		618 (35.8)		329 (39.4)		289 (32.5)
Marital status	4		2		2	
Partnered		1328 (76.7)		695 (83.0)		633 (70.7)
Unpartnered		404 (23.3)		142 (17.0)		262 (29.3)
Having children			2		1	
One or more				652 (77.9)		625 (69.8)
No				185 (22.1)		271 (30.3)
Diabetes[b]	0		0		0	
Yes		34 (2.0)		16 (1.9)		18 (2.0)
No		1702 (98.0)		823 (98.1)		879 (98.0)
Hypercholesterolemia[c]	1		1		0	
Yes		493 (28.4)		320 (38.2)		173 (19.3))
No		1242 (71.6)		518 (61.8)		724 (80.7)
Systolic blood pressure mmHg, mean (SD)	48	118.2 (13.7)	16	123.4 (12.9)	32	113.2 (12.6))
Systolic blood pressure ≥140 mmHg	48		16		32	
Yes		111 (6.6)		89 (10.8)		22 (2.5)
No		1577 (93.4)		734 (89.2)		843 (97.5)
Diastolic blood pressure mmHg, mean (SD)	48	76.7 (9.5)	16	80.1 (9.0)	32	73.4 (8.8)
Diastolic blood pressure ≥90 mmHg	48		16		32	
Yes		169 (10.0)		122 (14.8)		47 (5.4)
No		1519 (90.0)		701 (85.2)		818 (94.6)
Hypertension status[d]	22		13		9	
Yes		298 (17.4)		206 (24.9)		92 (10.4)
No		1416 (82.6)		620 (75.1)		796 (89.6)
Pulse pressure mmHg, mean (SD)	48	41.5 (8.7)	16	43.3 (9.2)	32	39.8 (7.8)
Pulse pressure ≥60 mmHg	48		16		32	
Yes		46 (2.7)		34 (4.1)		12 (1.4)
No		1642 (97.3)		789 (95.9)		853 (98.6)
Waist circumference cm, mean (SD)	50	84.4 (12.3)	17	92.2 (9.5)	33	76.9 (9.6)
High waist circumference[e]	50		17		33	
Yes		229 (13.6)		124 (15.1)		105 (12.2)
No		1457 (86.4)		698 (84.9)		759 (87.9)

Body Mass Index kg/m^2, mean (SD)	18	25.3 (3.9)	8	26.2 (3.4)	10	24.4 (4.2)
Body Mass Index ≥25 kg/m^2	18		8		10	
Yes		843 (49.1)		520 (62.6)		323 (36.4)
No		875 (50.9)		311 (37.4)		564 (63.6)
Alcohol abuse[f]	4		1		3	
Yes		106 (6.1)		61 (7.3)		45 (5.0)
No		1626 (93.9)		777 (92.7)		849 (95.0)
Daily smoking	4		1		3	
Yes		200 (11.6)		91 (10.9)		109 (12.2)
No		1532 (88.5)		747 (89.1)		785 (87.8)
Physical activity[g]	4		1		3	
Yes		898 (51.9)		465 (55.5)		433 (48.4)
No		834 (48.2)		373 (44.5)		461 (51.6)
Psychological distress score, mean (STD)			6	15.3 (11.4)	7	19.0 (12.5)
High psychological distress score[h]	13		6		7	
Yes		381 (22.1)		143 (17.2)		238 (26.7)
No		1342 (77.9)		690 (82.8)		652 (73.3)
Hours worked per week for the organization	24		13		11	
≤40		1601 (93.5)		748 (90.6)		853 (96.3)
> 40		111 (6.5)		78 (9.4)		33 (3.7)
Hours worked per week for another organization	30		10		20	
0		1477 (86.6)		698 (84.2)		779 (88.8)
≥ 1		229 (13.4)		131 (15.8)		98 (11.2)
Employee status, T3 (2015-2018)	2		1		1	
Yes		507 (29.2)		230 (27.5)		277 (30.9)
No		1222 (70.5)		606 (72.3)		616 (68.8)
Imprecise		5 (0.3)		2 (0.24)		3 (0.33)
Personal history of cardiovascular disease[i]	8		1		7	
Yes		101 (5.8)		54 (6.4)		47 (5.3)
No		1627 (94.2)		784 (93.6)		843 (94.7)
Family history of cardiovascular disease[j]	34		15		19	
Yes		784 (46.1)		356 (43.2)		428 (48.8)
No		897 (52.7)		460 (55.8)		437 (49.8)
Don't know		21 (1.23)		8 (1.0)		13 (1.5)
Gaziano's predicted cardiovascular risk score	53		18		35	
Low				639 (77.8)		814 (94.4)
Moderate or High				182 (22.2)		48 (5.6)

[a] Canadian dollars
[b]Diabetes was measured by the item *"has a doctor ever told you that you have diabetes?"*
[c]Hypercholesterolemia was measured by the item "has a doctor, nurse or other health care professional ever told you that your cholesterol level is too high?"
[d]Hypertension status refer to participants who had high BP or those who reported taking medication to lower their blood pressure.
[e] High waist circumference ≥ 88 cm (in women) or ≥ 102 cm (in men)
[f]10 or more drinks a week in women or 15 or more drinks a week in men
[g] Performed leisure physical activity for 20 to 30 minutes per session at least twice a week
[h] Psychological distress score greater than or equal to the highest quintile (score > 26.19)
[i]Personal history of angina pectoris, unstable angina, acute myocardial infarction, coronary bypass surgery, percutaneous coronary intervention, stroke
[j]A member of the immediate family (father, mother, brother, or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, hemorrhage, thrombosis) under the age of 60 years.

Table 2. Arterial stiffness at T3 (2015-2018) in men and women according to main cardiovascular diseases risk factors and psychosocial work-related factor at T2 (1999-2001)

	All 1736		Men 839		Women 897	
	N[a]	8.1 (1.7)	N[a]	8.6 (1.9)	N[a]	7.7 (1.4))
Age y						
<55	1602	8.0 (1.5)	750	8.4 (1.7)	852	7.7 (1.3)
≥55	134	9.7 (2.3)	89	10.0 (2.6)	45	9.1 (1.5)
Systolic blood pressure, mmHg						
<140	1625	8.1 (1.6)	750	8.5 (1.8)	875	7.7 (1.4)
≥140	111	9.2 (1.9)	89	9.4 (1.9)	22	8.7 (1.7)
Diastolic blood pressure mmHg						
<90	1567	8.1 (1.7)	717	8.5 (1.9)	850	7.7 (1.4)
≥90	169	8.9 (1.7)	122	9.1 (1.7)	47	8.4 (1.5)
Hypertension status[b]						
Yes	298	8.9 (1.9)	206	9.2 (2.0)	92	8.4 (1.6)
No	1416	8.0 (1.6)	620	8.4 (1.8)	796	7.7 (1.3)
High Pulse pressure[c], (> 60 mmHg)						
Yes	46	9.4 (2.3)	34	9.43 (2.4)	12	9.2 (2.0)
No	1642	8.1 (1.7)	789	8.5 (1.8)	853	7.7 (1.4)
Diabetes[d]						
Yes	34	9.7 (3.0)	16	11.3 (3.5)	18	8.3 (1.6)
No	1702	8.1(1.6)	823	8.5 (1.8)	879	7.7 (1.4)
Hypercholesterolemia[e]						
Yes	493	8.5 (1.8)	320	8.8 (1.9)	173	7.9 (1.4)
No	1242	8.0 (1.6)	518	8.4 (1.8)	724	7.7 (1.4)
High waist circumference[f]						
Yes	229	8.6 (1.8)	124	9.0 (2.1)	105	8.0 (1.3)
No	1457	8.1 (1.7)	715	8.5 (1.8)	792	7.7 (1.4)
Body Mass Index kg/m^2, mean (SD)						
<25	893	7.9 (1.5)	319	8.4 (1.7)	574	7.7 (1.4)
≥25	843	8.4 (1.8)	520	8.7 (1.9)	323	7.9 (1.4)
Daily smoking						
Yes	200	8.3 (1.7)	91	8.7 (1.9)	109	7.9 (1.4)
No	1532	8.1 (1.7)	747	8.5 (1.8)	785	7.7 (1.4)
Physical activity[g]						
Yes	898	8.1 (1.7)	465	8.5 (1.8)	433	7.6 (1.4)
No	834	8.2 (1.7)	373	8.7 (1.9)	461	7.8 (1.4)
Gaziano's predicted cardiovascular risk score						
Low	1453	7.9 (1.5)	639	8.3 (1.6)	814	7.7 (1.3)
Moderate or High	230	9.5 (2.1)	182	9.6 (2.2)	48	9.1 (1.6)
Number of accumulated cardiovascular risk factors						
0-1	1489	8.0 (1.6)	690	8.4 (1.7)	799	7.7 (1.4)
2+	194	9.1 (2.1)	131	9.4 (2.3)	63	8.4 (1.6)
Family history of cardiovascular disease[h]						
Yes	784	8.2 (1.7)	356	8.6 (1.9)	428	7.8 (1.4)
No	897	8.1 (1.6)	460	8.5 (1.8)	437	7.6 (1.3)
Don't know	21	7.7 (1.8)	8	8.4 (2.5)	13	7.3 (1.2)
Job strain						
Low strain	298	8.3 (1.8)	174	8.7 (1.9)	124	7.8 (1.4)
Passive	592	8.1 (1.7)	237	8.6 (1.8)	355	7.7 (1.5)
Active	486	8.2 (1.8)	280	8.4 (2.0)	206	7.8 (1.4)
High strain	344	8.0 (1.4)	141	8.5 (1.6)	203	7.6 (1.2)
Effort-reward imbalance						
Yes	408	8.2 (1.7)	197	8.6 (1.9)	211	7.8 (1.4)
No	1281	8.1 (1.7)	618	8.6 (1.9)	663	7.7 (1.4)

Arterial stiffness (m/s) in different subgroups are presented as mean and standard deviation (SD)
aThe number of observations used
b Hypertension status refer to participants who had high BP or those who reported taking medication to lower their blood pressure.
cPulse pressure = systolic blood pressure – diastolic blood pressure
dDiabetes was measured by the item *"has a doctor ever told you that you have diabetes?"*
eHypercholesterolemia was measured by the item "has a doctor, nurse or other health care professional ever told you that your cholesterol level is too high?"
fHigh waist circumference: ≥ 88 cm (in women) or ≥ 102 cm (in men)
g Performed leisure physical activity for 20 to 30 minutes per session at least twice a week
h A member of the immediate family (father, mother, brother, or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, hemorrhage, thrombosis) under the age of 60 years.

Table 3. Arterial stiffness (m/s) mean differences at T3 (2015-2018) and 95% confidence intervals according to psychosocial work-related factors at T2 (1999-2001) in men and women

	Modele I	Modele II	Modele III	Modele IV
Job strain in men				
Missing values/785 observations read	6	28	55	79
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	+0.04 (-0.26;+0.33)	+0.11 (-0.19;+0.41)	+0.16 (-0.15;+0.47)	+0.19 (-0.13;+0.51)
Active	-0.11 (-0.51;+0.29)	-0.14 (-0.50;+0.23)	-0.14 (-0.51;+0.23)	-0.05 (-0.42;+0.31)
High job strain	-0.07 (-0.68;+0.53)	+0.04 (-0.50;+0.58)	-0.05 (-0.61;+0.51)	-0.02 (-0.55;+0.50)
Job strain in women				
Missing values /850 observations read	9	44	86	110
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	-0.09 (-0.35;+0.18)	-0.21 (-0.44;+0.02)	-0.20 (-0.42;+0.03)	-0.23 (-0.47;+0.00)
Active	-0.03 (-0.31;+0.24)	-0.06 (-0.31;+0.18)	-0.03 (-0.30;+0.24)	-0.11 (-0.39;+0.16)
High job strain	-0.14 (-0.47;+0.20)	-0.25 (-0.54;+0.03)	-0.20 (-0.53;+0.13)	-0.27 (-0.59;+0.06)
Effort-Reward Imbalance in men				
Missing values /785 observations read	22	44	68	79
ERI (categorical variable)				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.22;+0.47)	+0.02 (-0.27;+0.31)	-0.07 (-0.39;+0.24)	-0.04 (-0.35;+ 0.28)
ERI (continuous variable)	+0.21 (-0.75;+1.17)	-0.06 (-0.89;+0.76)	-0.27 (-1.19;+0.66)	-0.16 (-1.20;+0.89)
Effort-Reward Imbalance in women				
Missing values /850 observations read	21	53	94	110
ERI				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.14;+ 0.39)	+0.05 (-0.16;+0.27)	+0.13 (-0.10;+0.36)	+0.18 (-0.08;+ 0.43)
ERI (continuous form)	+0.17 (-0.36;+0.69)	-0.04 (-0.46;+0.38)	+0.12 (-0.25;+0.49)	+0.18 (-0.28;+0.64)

Model I: unadjusted;
Model II: I+ age, education, income, marital status, children, familial history of cardiovascular disease at time T2 (1999-2001)
Model III: II+ systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, body mass index (Kg/m^2), waist circumference (cm), lifestyle (alcohol abuse, daily smoking, physical activity), psychological distress score at time T2.
Model IV: III+ hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance) at time T2.
Models are restricted to people with no personal history of cardiovascular disease at time T2.
ERI: effort-reward imbalance

Table 4. Arterial stiffness (m/s) mean differences at T3 (2015-2018) and 95% confidence intervals according to psychosocial work-related factors at T2 (1999-2001) stratified by blood pressure at the time of exposure

	Systolic Blood pressure, mmHg		Diastolic Blood pressure, mmHg		Pulse pressure, mmHg	
	<140	≥140	<90	≥90	≤60	> 60
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
Job strain						
Low strain	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Passive	-0.02 (-0.23;+0.19)	-0.27 (-1.28;+0.74)	-0.05 (-0.28;+0.18)	+0.03 (-0.72;+0.79)	-0.06 (-0.27;+0.14)	+1.54 (-0.47;+3.55)
Active	-0.05 (-0.28;+0.18)	-0.13 (-1.05;+0.80)	-0.08 (-0.33;+0.16)	+0.43 (-0.18;+1.04)	-0.09 (-0.31;+0.13)	**+2.06 (+0.69;+3.44)**
High job strain	-0.17 (-0.40;+0.07)	+0.84 (-0.35;+2.03)	**-0.25 (-0.48;-0.02)**	**+1.38 (+0.57;+2.19)**	-0.16 (-0.40;+0.08)	**+3.00 (+1.18;+4.76)**
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
ERI						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.08;+0.34)	**-1.17 (-2.12;-0.22)**	+0.11 (-0.12;+0.35)	-0.48 (-1.10;+0.14)	+0.08 (-0.10;+0.27)	**-2.06 (-3.33;-0.79)**
ERI (continuous form)	-0.02 (-0.55;+0.50)	+0.66 (-1.44;+2.77)	-0.04 (-0.57;+0.50)	-0.34 (-1.99;+1.31)	-0.04 (-0.56;+0.48)	+0.43 (-4.69;+5.55)

Models are adjusted for sex and covariates at time T2 (age, education, income, marital status, children, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, body mass index (Kg/m^2), waist circumference (cm), alcohol abuse, daily smoking, physical activity, familial history of cardiovascular disease, psychological distress, hours worked per week for the organization, hours worked per week for another organization, ERI (when studying the effect of job strain) or job strain (when studying the effect of ERI).
Models are restricted to people with no personal history of cardiovascular disease at time T2 (1999-2001).
Pulse pressure = systolic blood pressure – diastolic blood pressure
ERI: effort-reward imbalance

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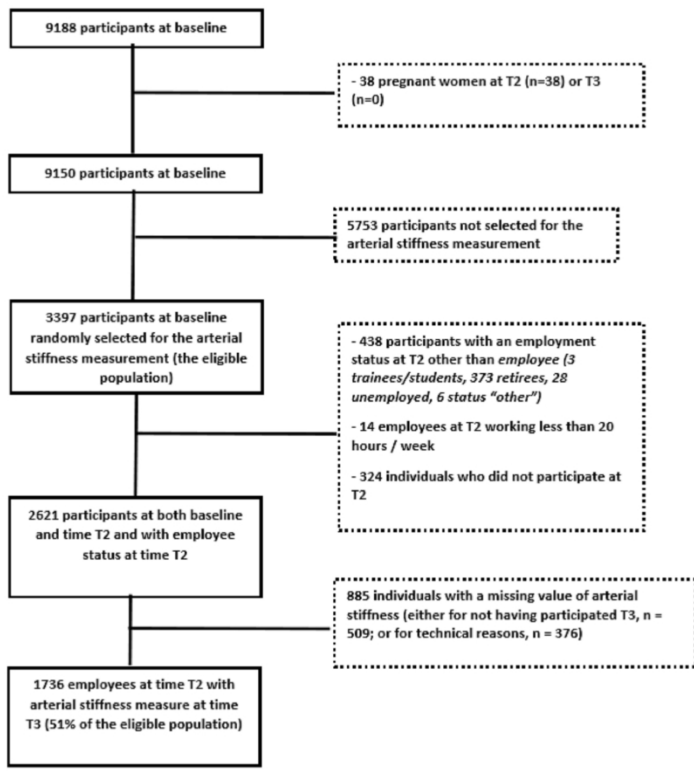
Figure 1. Flow chart



Baseline: 1991-1993; T2: 1999-2001; T3: 2015-2018

219x283mm (300 x 300 DPI)

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Table S1. Arterial stiffness (cfPWV in m/s) mean differences at time T3 and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at time T2 stratified by age and Gaziano's predicted cardiovascular risk at the time of exposure

	Age, years		Gaziano's predicted cardiovascular risk	
	<55	≥55	Weak	Moderate or high
Missing/observations read	162/1523	27/112	110/1383	28/201
Job strain				
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	-0.06 (-0.29;+0.17)	+0.25 (-0.74;+1.23)	-0.10 (-0.33;+0.13)	+0.30 (-0.34;+0.94)
Active	-0.07 (-0.31;+0.17)	+0.26 (-0.68;+1.21)	-0.08 (-0.33;+0.17)	+0.16 (-0.40;+0.72)
High job strain	-0.11 (-0.35;+0.14)	+0.55 (-1.23;+2.34)	-0.13 (-0.37;+0.11)	+0.24 (-0.55;+1.03)
Missing/observations read	162/1523	27/112	110/1383	28/201
ERI				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.06 (-0.13;+0.25)	+0.52 (-0.67;+1.71)	+0.08 (-0.11;+0.28)	-0.20 (-0.77;+0.37)
ERI (continuous form)	+0.04 (-0.46;+0.54)	-0.32 (-3.25;+2.62)	+0.04 (-0.53;+0.60)	-0.21 (-1.54;+1.12)

Models are adjusted for sex and covariates at time T2 (age, education, income, marital status, children, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, BMI, waist circumference (cm), alcohol abuse, daily smoking, physical activity, familial history of cardiovascular disease, psychological distress, hours worked per week for the organization, hours worked per week for another organization, ERI (when studying the effect of job strain) or job strain (when studying the effect of ERI).
Models are restricted to people with no personal history of cardiovascular disease at time T2T2.
ERI: effort-reward imbalance
cfPWV: carotid-femoral pulse wave velocity
Time T2: 1999-2001; time T3: 2015-2018
The Gaziano's predicted cardiovascular risk is a non-laboratory-based method for assessment of cardiovascular disease using the following cardiovascular risk factors: sex, age, diabetes, systolic blood pressure, smoking and body mass index (1, 2)

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Table S2a. Arterial stiffness (cfPWV in m/s) mean differences at time T3 and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at time T2 stratified by employment status at the time of arterial stiffness measurement (fully adjusted model*)

	Employees	Non-employees
Missing/observations read	49/492	139/1137
Job strain		
Low strain	Ref	Ref
Passive	-0.04 (-0.24;+0.16)	-0.05 (-0.28;+0.19)
Active	-0.18 (-0.52;+0.16)	+0.04 (-0.29;+0.36)
High job strain	+0.00 (-0.33;+0.34)	-0.14 (-0.41;+0.13)
Missing/observations read	49/492	139/1137
ERI		
No	Ref	Ref
Yes	+0.13 (-0.12;+0.37)	+0.05 (-0.23;+0.34)
ERI (continuous form)	+0.43 (-0.33;+1.18)	-0.04 (-0.70;+0.61)

*The model is adjusted for covariates at time T2 (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).) and for gender
People with personal history of cardiovascular events at time T2 are not included.
ERI: effort-reward imbalance
The category of people with imprecise employment status was excluded from stratification given a low size.
Time T2: 1999-2001; time T3: 2015-2018

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Table S2b. Arterial stiffness (m/s) mean differences at time T3 and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at time T2 in participants with the status of retired in time T3 according to the duration of the retirement (fully adjusted model*)

	The duration of the retirement	
	≤ 2 years	> 2 years
Missing/observations read	34/293	90/778
Job strain		
Low strain	Ref.	Ref.
Passive	+0.07 (-0.34;+0.49)	-0.10 (-0.40;+0.19)
Active	-0.14 (-0.54;+0.27)	-0.04 (-0.36;+0.29)
High job strain	-0.24 (-0.69;+0.22)	-0.20 (-0.58;+0.19)
Missing/observations read	34/293	90/778
ERI		
No	Ref	Ref
Yes	+0.03 (-0.30;+0.35)	+0.20 (-0.14;+0.55)
ERI (continuous form)	-0.26 (-0.91;+0.38)	+0.29 (-0.61 ;+1.19)

The model is adjusted for covariates at time T2 (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance)) and for gender
People with personal history of cardiovascular events at time T2 are not included.
ERI: effort-reward imbalance
Time T2: 1999-2001; time T3: 2015-2018

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Table S3. Arterial stiffness (m/s) mean differences at time T3 and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at time T2 with and without participants with personal history of cardiovascular events* at baseline (fully adjusted models)

Exposure	With individuals with personal history of CVD at T2 (Model A)	Without individuals with personal history of CVD at T2 (Model B)
Job strain in men		
Low strain	Ref.	Ref.
Passive	+0.21 (-0.10;+0.51)	+0.19 (-0.13;+0.51)
Active	-0.11 (-0.45;+0.24)	-0.05 (-0.42;+0.31)
High job strain	-0.02 -0.57;+0.52)	-0.02 (-0.55;+0.50)
Job strain in women		
Low strain	Ref.	Ref.
Passive	-0.18 (-0.40;+0.05)	-0.23 (-0.47;+0.00)
Active	-0.03 (-0.34;+0.28)	-0.11 (-0.39;+0.16)
High job strain	**-0.30 (-0.57;-0.02)**	-0.27 (-0.59;+0.06)
Effort-reward imbalance in men		
No	Ref.	Ref.
Yes	-0.09 (-0.43;+ 0.26)	-0.04 (-0.35;+ 0.28)
Effort-reward imbalance in women		
No	Ref.	Ref.
Yes	+0.22 (-0.10;+ 0.53)	+0.18 (-0.08;+ 0.43)

* Cardiovascular events: angina pectoris, acute myocardial infarction, coronary bypass surgery, dilation
Model A includes covariates at time T2 (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, personal history of CVD , psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).).
Model B= Model A without participants with personal history of cardiovascular events at time T2 (n=101)
Baseline: 1991-1993; time T2: 1999-2001; time T3: 2015-2018

Article _ supplement Association between psychosocial work-related factors exposures assessed at midlife and arterial stiffness at older age among 1,736 white-collar workers

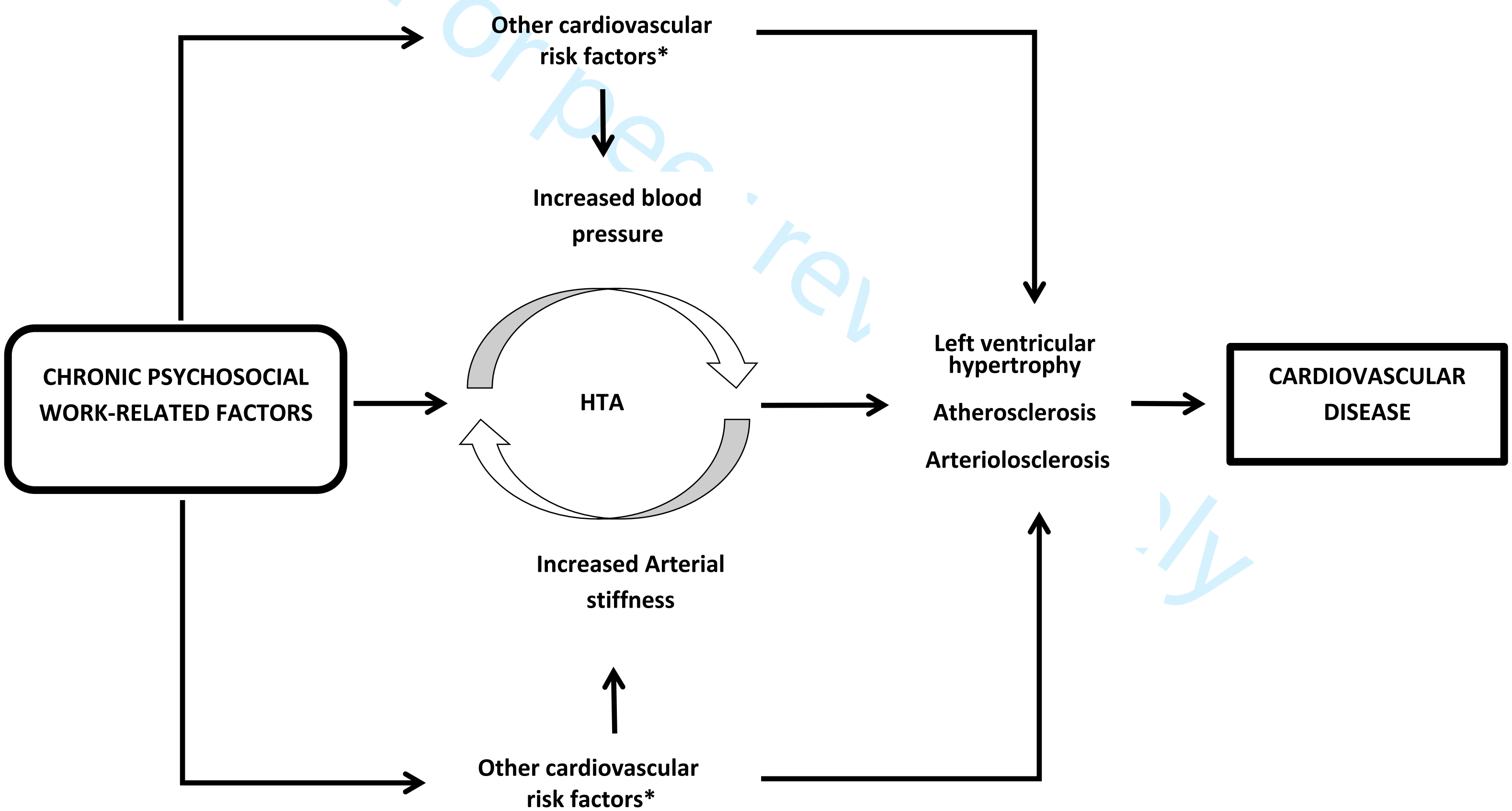
Table S4. Arterial stiffness (m/s) mean differences at time T3 and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at time T2 before and after correction for selection bias (fully adjusted models*)

	Men			Women		
	No imputation	42 imputations	IPW	No imputations	42 imputations	IPW
Job strain at T2						
Low strain	Ref.	Ref.	Ref..	Ref.	Ref.	Ref.
Passive	+0.19 (-0.13;+0.51)	+0.10 (-0.19;+0.39)	+0.10 (-0.27;+0.47)	*-0.23 (-0.47;+0.00)*	-0.19 (-0.44;+0.06)	-0.12 (-0.49;+0.24)
Active	-0.05 (-0.42;+0.31)	-0.06 (-0.39;+0.28)	+0.01 (-0.43;+0.44)	-0.11 (-0.39;+0.16)	-0.10 (-0.37;+0.16)	-0.08 (-0.49;+0.33)
High job strain	-0.02 (-0.55;+0.50)	-0.07 (-0.50;+0.36)	-0.05 (-0.59;+0.48)	-0.27 (-0.59;+0.06)	-0.25 (-0.59;+0.09)	-0.23 (-0.60;+0.14)
ERI						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	-0.04 (-0.35;+ 0.28)	+0.07 (-0.18;+0.32)	+0.21 (-0.11;+0.55)	+0.18 (-0.08;+ 0.43)	+0.09 (-0.13;+0.31)	+0.07 (-0.22;+0.36)
ERI (continuous form)	-0.16 (-1.20;+0.89)	+0.25 (-0.64;+1.14)	+0.29 (-0.72;+1.30)	+0.18 (-0.28;+0.64)	+0.13 (-0.43;+0.69)	+0.09 (-0.62;+0.80)

*Models are adjusted for covariates at time T2 (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).).
Models are restricted to people with no personal history of cardiovascular events at time T2
ERI: effort-reward imbalance
IPW: inverse probability weighting
Time T2: 1999-2001; time T3: 2015-2018

Article _ supplement Association between psychosocial work-related factors exposures assessed at midlife and arterial stiffness at older age among 1,736 white-collar workers

Figure S1. Possible sequences of events between chronic exposure to psychosocial work-related factors and the development of cardiovascular diseases, based on the cardiovascular continuum



* Adiposity, smoking, alcohol abuse, excessive salt intake, physical inactivity, dyslipidemia, diabetes, mental health, chronic inflammation.

Article _ supplement Association between psychosocial work-related factors exposures assessed at midlife and arterial stiffness at older age among 1,736 white-collar workers

References

1. Gaziano TA, Young CR, Fitzmaurice G, Atwood S, Gaziano JM. Laboratory-based versus non-laboratory-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort. Lancet (London, England). 2008;371(9616):923-31.
2. Pandya A, Weinstein MC, Gaziano TA. A comparative assessment of non-laboratory-based versus commonly used laboratory-based cardiovascular disease risk scores in the NHANES III population. PloS one. 2011;6(5):e20416-e.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1;2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5;6;7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5;6
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7;8
		(*d*) If applicable, explain how loss to follow-up was addressed	7;8
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8;14
		(b) Indicate number of participants with missing data for each variable of interest	14; Figure 1
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8;16

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7;8;18;19 15;17 No relative risk
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10;11;12;13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Figure 1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Association between psychosocial work-related factors at midlife and arterial stiffness at older age in a prospective cohort of 1,736 white-collar workers

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Association between psychosocial work-related factors at midlife and arterial stiffness at older age in a prospective cohort of 1,736 white-collar workers

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Key words: Psychosocial work-related factors, arterial stiffness, blood pressure, prevention.

Number of words: 3,090 (from the introduction to the conclusion, excluding title page, abstract, references, figures and tables)

Abstract

Objective Arterial stiffness and exposure to psychosocial work-related factors increase the risk of developing cardiovascular disease (CVD). However, little is known about the relationship between psychosocial work-related factors and arterial stiffness. We aimed to examine this relationship.

Design Prospective cohort study.

Setting Public organizations in Quebec City, Canada.

Participants The study included 1,736 white-collar workers (women 52%) from 19 public organizations.

Primary and secondary outcome measures Association between psychosocial work-related factors from the job strain and effort-reward imbalance (ERI) models assessed at study baseline (1999-2001) with validated instruments and arterial stiffness assessed using carotid-femoral pulse wave velocity at follow-up, on average 16 years later (2015-2018). Generalized estimating equations were used to estimate differences in arterial stiffness between exposed and unexposed participants. Subgroup analyses according to sex, age, blood pressure (BP), cardiovascular risk score and employment status were conducted.

Results Among participants with high diastolic BP (≥90 mmHg) at baseline, aged 47 on average, those exposed to high job strain had higher arterial stiffness (+1.38 m/s (95% CI: +0.57; +2.19)) at follow-up, 16 years later, following adjustment for a large set of potential confounders. The trend was similar in participants with high systolic BP (≥140 mmHg) exposed to high job strain (+0.84 m/s (95% CI: -0.35; +2.03)). No association was observed for ERI in the total sample and counterintuitive associations were observed in subgroup analyses.

Conclusions Job strain may have a long-term deleterious effect on arterial stiffness in people with high BP. Interventions at midlife to reduce job strain may mitigate arterial stiffness progression.

Strengths and limitations of this study

- This study has a long follow-up period of 16 years.
- Arterial stiffness was measured using carotid-femoral pulse wave velocity, the gold standard.
- Psychosocial work-related factors were assessed using validated instruments.
- This study examines the effect of psychosocial work-related factors measured at a single point in time.

Introduction

Cardiovascular disease (CVD) is a major public health problem. CVD develops over several years across a continuum initiated by one or several risk factors, which can progress to atherosclerosis, cardiovascular events and end-stage organ disease (1). The main modifiable risk factors for CVD include dyslipidemia, high blood pressure (BP), smoking, diabetes and adiposity. Additional factors such as psychosocial work-related factors can contribute to increase the risk of CVD (2). In Organisation for Economic Co-operation and Development countries, 20-25% of workers are exposed to adverse psychosocial work-related factors (3).

Arterial stiffness describes the reduced ability of large proximal arteries to dilate and retract. Carotid-femoral pulse wave velocity (cfPWV), the gold standard method for assessing aortic stiffness, is linearly associated with CVD risk (4). An increase in aortic pulse wave velocity of 1 m/s corresponds to an adjusted risk increase of 14% in fatal or nonfatal cardiovascular events (4). Adverse psychosocial work-related factors may be associated with high arterial stiffness. Results of prior studies differ according to types of exposure and sex, suggesting deleterious (5-9), beneficial (10) or no effect (11) of psychosocial work-related factors on arterial stiffness. All prior studies are limited by their cross-sectional design. None used the gold standard measure for arterial stiffness.

The objective of the present study was to examine the association between psychosocial work-related factors and arterial stiffness in a prospective cohort study of men and women from Quebec City, Canada. Men and women were considered separately since the prevalence of psychosocial work-related factors and their effects differ by sex (2). Elevated midlife BP is associated with increased arterial stiffness (12). The relationship between midlife psychosocial work-related factors and arterial stiffness might therefore vary between people with and without elevated BP. This potential effect modification was examined.

Methods

Population and study design

We used data from a prospective cohort study. This cohort was initiated in 1991-1993 among 9,188 white-collar workers (participation proportion: 75%) from 19 public organizations in Quebec City with two subsequent phases of data collection (1999-2001 and 2015-2018) (13). The current study baseline was set in 1999-2001, since ERI exposure was firstly assessed at that time. Arterial stiffness was assessed at follow up (2015-2018). Among the 9,188 participants in the original cohort initiation, 8,120 (88.4 %) and 6,707 (73 %) participated at 1999-2001 and 2015-2018, respectively. Arterial stiffness was measured in 1/3 of participants randomly selected. For the present study, baseline corresponds to the 1999-2001 period and follow-up time to 2015-2018. The study sample included 1,736 participants with employee status at baseline (Figure 1). The *Centre Hospitalier Universitaire de Québec – Université Laval* (CHUdeQc-UL) ethical research committee (2012-1674; DR-002-1409; F9H-63202) approved the study. All participants signed an informed consent form.

Data collection

At each wave, workers completed a self-administered questionnaire on risk factors for hypertension and CVD, demographic, occupational and social characteristics. Trained staff measured BP (using the mercury sphygmomanometer at baseline and the automated BP-TRU device (VSM MedTech, Coquitlam, Canada) at follow-up), height, weight, and waist circumference. Arterial stiffness was measured at follow-up.

Psychosocial work-related factors

Job strain and effort-reward imbalance (ERI) exposures were assessed at baseline (1999-2001). Components of job strain (psychological demands and job control) were measured using 18 items from the Job Content Questionnaire (14). Psychological demands include the quantity of work, time constraints and level of intellectual effort. Job control includes opportunities for learning, autonomy, and participation in the decision-making process. The theoretical model postulates that the greatest health risk occurs in workers combining high demands and low control. The psychometric properties of the original English (15) and French (16) questionnaires have been demonstrated. We classified workers with demands scores≥24 (the median in the Quebec working population) in the *high demands* group and those with control scores≤72 (the median in the Quebec working population) in the *low control* group. The *low strain* group included workers combining *low demands* and *high control*. The p*assive*, *active* and *high strain* groups included respectively people combining *low demands* and *low control*, *high demands* and *high control* and *high demands* and *low control*.

The ERI model states that efforts should be rewarded with income, respect and esteem, and occupational status control. Workers are in a state of deleterious imbalance when high efforts are accompanied by low reward, and are more susceptible to health problems. The modified French version of the questionnaire was used to assess ERI. Reward at work was measured by nine original questions from the French version (17) of the ERI scale. Effort was measured by nine items from the validated French version of the psychological demand scale of the Job Content Questionnaire (18). The psychometric qualities of this ERI scale version have been demonstrated (19). Effort and reward scores were computed with the sum of items. A ratio efforts/reward>1 indicated an imbalance. The ratio was also used in its continuous form.

Arterial stiffness as cfPWV (m/s)

Arterial stiffness was measured at follow-up using the Complior Analyse device (Alam Medical, Saint-Quentin-Fallavier, France). The transit time between the carotid and the femoral pulse was measured twice in each participant. cfPWV was calculated by dividing the carotid-femoral transit distance (calculated using the difference in body surface measurements from the suprasternal notch to the femoral and carotid sites) by the carotid-femoral transit time delay. A third measurement was taken if the difference between the two measurements was >0.5 m/s. Inter- and intra-observer reproducibility of this measurement has been reported as excellent (20).

Covariates

Potential confounders included the following risk factors for arterial stiffness: demographic characteristics (age, sex, education, household income, marital status and having children); biological factors (BP, body mass index (BMI), waist circumference, diabetes, hypercholesterolemia and personal history of cardiovascular event), lifestyle factors (daily smoking, alcohol abuse and leisure time physical activity); family history of

CVD at ≤ 60 years of age; psychological distress (Psychiatric Symptom Index); other work factors (hours worked for the organization, hours worked for another organization).

Statistical analyses

Continuous data were expressed as the mean along with the standard deviation. Categorical data were expressed as number and percentages. Generalized estimating equations were used to estimate differences in arterial stiffness means between the exposed and unexposed groups, with their 95% confidence interval (21). Regression models accounted for the correlation between employees of the same organization. The models were sequentially adjusted for sets of covariates given that biological factors, psychological distress and lifestyle factors potentially mediate the associations (Figure 2). As job strain and ERI models provide distinct information, we assessed the independent effect of job strain and ERI by adjusting for job strain when measuring the association with ERI and vice versa. In order to assess effect modification, we conducted subgroup analyzes by sex and BP (systolic, diastolic and pulse pressure) at baseline. Sensitivity analyses were also conducted i) with and without individuals with personal history of CVD since they may have increased arterial stiffness; ii) according to risk factors for arterial stiffness at baseline (age and Gaziano's cardiovascular risk score (22)) since they may increase the deleterious effects of psychosocial work-related factors (23); iii) according to job status at follow-up since retirement may attenuate the effects of psychosocial work-related factors (24). Multiple imputations (25) and inverse probability weighting (26) were performed to minimize potential selection bias due to non-response and/or loss to follow-up. Covariates measured at the initiation of the original cohort (in 1991-1993) were used in the calculation of the weights that were used for inverse probability weighting in order to minimize the potential selection bias resulting from losses to follow-up between cohort initiation and subsequent time points.

Analyses were performed with SAS 9.4 software. The level of statistical significance was set at 0.05.

Participant and public involvement

Participants or the public were not involved in the study design, conduct, reporting, or dissemination plans.

Results

Mean follow-up time between exposure (baseline) and arterial stiffness assessment (follow-up) was 16.8 (standard deviation: 1.3) years. At baseline, participants were on average 45 years old. More women (23%) than men (17%) were exposed to high job strain. As many men as women were exposed to ERI (24%). At follow-up, participants were on average 62 years old (Table 1).

Table 2 presents mean arterial stiffness at follow-up in men and women according to main risk factors for cardiovascular diseases and psychosocial work-related factor at baseline. Arterial stiffness (mean:8.1± 1.7 m/s) was higher in men, in older participants and among those with high BP, diabetes, hypercholesterolemia, high waist circumference, high BMI and moderate or high cardiovascular risk score.

Table 3 presents the association between psychosocial work-related factors at baseline and arterial stiffness at follow-up. In men, arterial stiffness was slightly higher in those with passive jobs. In women, arterial stiffness was higher in participants exposed to ERI. All differences were modest and not statistically significant, with confidence intervals including the null value.

Table 4 presents the association between psychosocial work-related factors and arterial stiffness according to BP at baseline. The high job strain group had higher arterial stiffness (+1.38 m/s (95%CI: +0.57; +2.19)) among participants with high diastolic BP (≥90 mmHg) and lower arterial stiffness (-0.25 (95%CI: -0.48;-0.02)) among those with lower diastolic BP (<90 mmHg). The same trend was observed for systolic BP. The high job strain group had higher arterial stiffness (+0.84 m/s (95% CI: -0.35; +2.03), p=0.17) among those with systolic BP≥140 mmHg. Arterial stiffness was also higher in the high job strain (+3.00 (95%CI: +1.18;+4.76)) and the passive (+2.06 (95%CI: +0.69;+3.44)) groups among participants with pulse pressure>60 mmHg. However, only 43 participants had high pulse pressure. ERI was associated with lower arterial stiffness in participants with systolic BP≥140 mmHg (-1.17 (95%CI:-2.12;-0.22)), in those with diastolic BP≥90 mmHg (-0.48 (95%CI:-1.10;+0.14)) and with pulse pressure>60 mmHg (-2.06 (95%CI:-3.33;-0.79)) (Table 4).

Supplementary analyses showed that arterial stiffness tended to be higher in participants exposed to job strain who were ≥55 years old or had a moderate or high CVD risk score. The ERI group had higher arterial stiffness in the 55+ age stratum (+0.52 (95%CI:-0.67;+1.71) (Table S1, supplement). Psychosocial work-related factors were not associated with arterial stiffness when stratifying according to employment status and duration of retirement (Table S2a and S2b, supplement). The findings were similar with and without participants with history of CVD (Table S3, supplement), and before and after multiple imputation and inverse probability weighting (Table S4, supplement).

Discussion

In the present study, arterial stiffness was not significantly higher in men and women exposed to high job strain and ERI overall. However, among participants with higher diastolic BP at midlife, high job strain was associated with higher arterial stiffness 16 years later. This association was robust to adjustment for socio-demographics, lifestyle-related risk factors, CVD risk factors and other factors from the work environment.

Prior studies assessing the relationship between psychosocial work-related factors and arterial stiffness were cross-sectional (5-11). Most suggest a deleterious effect (5-9). Studies suggesting a protective (10) or no effect (11) involved relatively young participants (≤40 years). Studies showing deleterious associations included people aged over 40 years on average (5-7, 9), a high proportion of smokers (>40%) (5, 6) or targeted workers in professions at higher risk of developing CVD such as firefighters (9). Given their cross-sectional design, previous studies do not inform on different aspects of the temporal relationship between psychosocial work-related factors and arterial stiffness, including the optimal time window and follow-up period. The time required between exposure to psychosocial work-related factors and arterial stiffness may vary according to the position of individuals on the cardiovascular continuum. A longer follow-up time could be required for participants who are at an earlier stage than for those who are at a more advanced stage of progression. In the present study, high job strain was associated with increased arterial stiffness 16 years later (+1.38 m/s), in participants with high diastolic BP at time of exposure assessment (baseline). The mean age of participants with high DBP at baseline was 47 years old. Given that diastolic hypertension predominates in relatively young individuals, at a relatively early stage of the cardiovascular continuum and that CVD develops over at least a decade, it is reasonable to postulate that the follow-up period used in the present study was appropriate for measuring the association between midlife work-related factors and arterial stiffness in participants with high DBP at midlife (12, 27).

Increased arterial stiffness was also observed among participants with high systolic BP. This association was however of smaller magnitude and did not reach statistical significance. This is consistent with the natural history of systolic/diastolic BP progression and its link with CVD diseases onset (27). On the contrary, high job strain was associated with reduced arterial stiffness in participants who did not have high BP. Measuring the association between midlife stressors and arterial stiffness among people who do not have high BP may require a longer follow-up, which could explain the presence of this counterintuitive protective association. This is consistent with a previous cross-sectional study which showed a protective association between job strain index and brachial-ankle PWV (-1.38 m/s, $p<0.01$). This previous study included young participants (median age: 31 years) with diastolic (median: 79 mmHg) and systolic (median: 110 mmHg) BP in the normal range (10). Further studies are needed to confirm these results.

Due to limited statistical power, caution should be exercised in interpreting the trends of increased arterial stiffness among participants exposed to job strain in moderate to high cardiovascular risk score and older participants' strata. These results should be regarded as hypothesis generating. In our study, the participants who remained actively employed at follow-up were relatively young (on average 39 years old) and had a low cardiovascular risk score (98%) at baseline. Younger age combined with low cardiovascular risk score may contribute to the absence of observed association. Indeed, among this younger subgroup, the timeframe for arterial stiffness assessment could have been suboptimal. ERI was associated with lower arterial stiffness in participants with high systolic BP, diastolic BP and high pulse pressure. This is counterintuitive and needs to be replicated.

In normotensive people without additional cardiovascular risk factors aged 60 to 69, the reference value for arterial stiffness is on average 10.3 m/s (28, 29). In the present study, the average value (8.3 m/s) of participants in this age group (n=930) is lower. The attrition due to non-response and loss to follow-up may have contributed to these finding given the loss of individuals who may be sicker than those who participated, as demonstrated in this cohort (30). As expected, participants at higher risk of CVD (men, older age, high BP, diabetes, hypercholesterolemia, high waist circumference, high BMI, moderate or high cardiovascular risk score) generally had higher arterial stiffness than those at lower risk. The observed association between psychosocial work-related factors and cfPWV can be translated into vascular age. For example, among participants with elevated DBP, those exposed to job strain (mean age: 63.1) had a mean cfPWV of 9.4 m/s, which is compatible with a vascular age of 50-59 years (28, 29). However, participants with elevated DBP in the low strain category (mean age: 64.9) had a mean cfPWV = 7.9 m/s, which is compatible with a vascular age of 30-39 years (28, 29). The observed difference in cfPWV among participants exposed to job strain within this subgroup is therefore compatible with a decade discrepancy in vascular age.

Chronic stress accelerates aging of arteries by incompletely understood mechanisms. Chronic stress can on one hand activate the sympathetic nervous system interconnected with the renin-angiotensin-aldosterone system and endothelin-1 activity and on the other hand promote risky lifestyle (31, 32). This leads to changes in vascular cell phenotypes and to thickening of the arterial innermost and intermediate layers, stiffness and increase in systolic and pulse pressure later on (31). Increased arterial stiffness causes excessive transmission of pulse pressure that can damage the microcirculation of target organs, which increases the risk of cardiovascular events (33). Older subjects or those with cardiovascular risk factors could have decreased endothelial regeneration capacity due to a reduced number of circulating progenitor endothelial cells (31, 34). A reduced regenerative capacity could explain a deleterious effect of job strain in people with an increased risk of developing a cardiovascular event given their age, cardiovascular risk score or high BP. Al Mheid et al. observed significant interactions ($P \leq 0.005$) between age and the burden of cardiovascular risk factors (smoking, diabetes mellitus, hypertension, or hyperlipidemia), such that for younger subjects (<40 years), cardiovascular risk factors were associated with increased progenitor cells counts, whereas for older subjects (>60 years), cardiovascular risk factors and CVD were associated with lower progenitor cells counts (34).

Our study has several strengths. To our knowledge, this is the first study to examine the association between psychosocial work-related factors assessed at midlife and arterial stiffness assessed at older age, using a prospective cohort. The 16-year follow-up allowed exploration of long-term effects. Other strengths are the use of a gold standard arterial stiffness measurement and validated psychosocial work-related factors models, sequential adjustment by several potentially confounding factors, inverse probability weighting to minimize the potential for selection bias and subgroup analyzes based on a priori evidence.

Our study has also limitations. First, the potential for selection bias due to a high proportion of missing values (40% out of 2,621 participants) and losses to follow-up (19% out of 2,621) may underestimate associations (30). However, the associations were similar before and after accounting for potential selection bias using multiple imputations and inverse probability weighting, suggesting that this potential bias could not have explained our results. Second, the use of a single measure of exposure limits the capacity to capture fluctuations in exposure and can lead to non-differential misclassification of exposure that may underestimate the association. Third, measuring arterial stiffness in 1/3 of participants combined with attrition reduced statistical power. Fourth, the study population was entirely composed of white-collar workers. Caution is therefore advised in generalizing to other types of occupations. The fact that our sample is composed exclusively of white-collar employees limits potential confounding by occupational physical burden (repetitive movements, lifting heavy loads, long walking distance …). Fifth, arterial stiffness was measured at a single time point (at follow-up only). Therefore, stiffness progression over time could not be assessed limiting the possibility to draw causal inferences. However, data on several other major cardiovascular risk factors (age, blood pressure, cholesterol, smoking, etc.) were controlled for, which minimized the possibility for participants in compared group to substantially differ regarding their overall cardiovascular profile at baseline.

Conclusion

Job strain exposure combined with high BP at midlife may have long-term deleterious effects on arterial stiffness. Interventions at midlife to reduce job strain may be considered as a potential way to manage CVD risk.

Data availability statement

Data cannot be shared publicly due to privacy concerns of study participants. However, data will be shared following a justified request to the corresponding author, conditional on permission from the *Centre Hospitalier Universitaire de Québec – Université Laval* (CHUdeQc-UL) ethical research committee.

Ethics statements

Patient consent for publication

Not applicable

Ethics approval

The study was approved by the *Centre Hospitalier Universitaire de Québec – Université Laval* (CHUdeQc-UL) ethical research committee (2012-1674; DR-002-1409; F9H-63202).

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Contributors

VKM conceptualized and designed the study, performed the statistical analysis, drafted, reviewed and edited the manuscript. CB was responsible for the study concept, supervised the data collection and the methodological aspects, reviewed and edited the manuscript. DT supervised the analytical approach, revised the statistical analysis program, reviewed and edited the manuscript. AM supervised aspects related to arterial stiffness, blood pressure and other cardiovascular risk factors, reviewed and edited the manuscript. XT supervised the methodological aspects, reviewed and edited the manuscript. MV, CED, BM, MGO, GRD and NP reviewed and edited the manuscript.

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Competing interests

Funders had no influence on study conduct and reporting. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Participant and public involvement

Participants or the public were not involved in the study design, conduct, reporting, or dissemination plans.

Table 1. Population characteristics at baseline (1999-2001) (unless otherwise stated) by sex

	Missing	All 1736 (100.0%)	Missing	Men 839 (48.3%)	Missing	Women 897 (51.7%)
Age y, mean (SD), cohort initiation (1991-1993)	0	37.3 (6.6)	0	38.6 (6.9)		36.2 (6.1)
Age y, mean (SD), baseline (1999-2001)	0	44.9 (6.7)	0	46.2 (7.0)	0	43.8 (6.2)
Age y, mean (SD), follow-up (2015-2018)	0	61.7 (6.1)	0	63.0 (6.4)		60.6 (5.6)
Job strain	16		7		9	
Low strain		298 (17.3)		174 (20.9)		124 (14.0)
Passive		592 (34.4)		237 (28.5)		355 (40.0)
Active		486 (28.3)		280 (33.7)		206 (23.2)
High strain		344 (20.0)		141 (17.0)		203 (22.9)
Effort-reward imbalance	47		24		23	
Yes		408 (24.2)		197 (24.2)		211 (24.1)
No		1281 (75.8)		618 (75.8)		663 (75.9)
Completed education	12		3		9	
Secondary or less		334 (19.4)		67 (8.0)		267 (30.1)
College (CEGEP)		530 (30.7)		238 (28.5)		292 (32.9)
University		860 (49.9)		531 (63.5)		329 (37.1)
Household income $C[a]	11		4		7	
0 - 49 999		426 (24.7)		144 (17.3)		282 (31.7)
50 000 - 79 999		681 (39.5)		362 (43.4)		319 (35.8)
≥ 80 000$		618 (35.8)		329 (39.4)		289 (32.5)
Marital status	4		2		2	
Partnered		1328 (76.7)		695 (83.0)		633 (70.7)
Unpartnered		404 (23.3)		142 (17.0)		262 (29.3)
Having children			2		1	
One or more				652 (77.9)		625 (69.8)
No				185 (22.1)		271 (30.3)
Diabetes[b]	0		0		0	
Yes		34 (2.0)		16 (1.9)		18 (2.0)
No		1702 (98.0)		823 (98.1)		879 (98.0)
Hypercholesterolemia[c]	1		1		0	
Yes		493 (28.4)		320 (38.2)		173 (19.3))
No		1242 (71.6)		518 (61.8)		724 (80.7)
Systolic blood pressure mmHg, mean (SD)	48	118.2 (13.7)	16	123.4 (12.9)	32	113.2 (12.6))
Systolic blood pressure ≥140 mmHg	48		16		32	
Yes		111 (6.6)		89 (10.8)		22 (2.5)
No		1577 (93.4)		734 (89.2)		843 (97.5)
Diastolic blood pressure mmHg, mean (SD)	48	76.7 (9.5)	16	80.1 (9.0)	32	73.4 (8.8)
Diastolic blood pressure ≥90 mmHg	48		16		32	
Yes		169 (10.0)		122 (14.8)		47 (5.4)
No		1519 (90.0)		701 (85.2)		818 (94.6)
Hypertension status[d]	22		13		9	
Yes		298 (17.4)		206 (24.9)		92 (10.4)
No		1416 (82.6)		620 (75.1)		796 (89.6)
Pulse pressure mmHg, mean (SD)	48	41.5 (8.7)	16	43.3 (9.2)	32	39.8 (7.8)
Pulse pressure ≥60 mmHg	48		16		32	
Yes		46 (2.7)		34 (4.1)		12 (1.4)
No		1642 (97.3)		789 (95.9)		853 (98.6)
Waist circumference cm, mean (SD)	50	84.4 (12.3)	17	92.2 (9.5)	33	76.9 (9.6)
High waist circumference[e]	50		17		33	
Yes		229 (13.6)		124 (15.1)		105 (12.2)
No		1457 (86.4)		698 (84.9)		759 (87.9)
Body Mass Index kg/m², mean (SD)	18	25.3 (3.9)	8	26.2 (3.4)	10	24.4 (4.2)

Body Mass Index ≥25 kg/m²	18		8		10	
Yes		843 (49.1)		520 (62.6)		323 (36.4)
No		875 (50.9)		311 (37.4)		564 (63.6)
Alcohol abuse[f]	4		1		3	
Yes		106 (6.1)		61 (7.3)		45 (5.0)
No		1626 (93.9)		777 (92.7)		849 (95.0)
Daily smoking	4		1		3	
Yes		200 (11.6)		91 (10.9)		109 (12.2)
No		1532 (88.5)		747 (89.1)		785 (87.8)
Physical activity[g]	4		1		3	
Yes		898 (51.9)		465 (55.5)		433 (48.4)
No		834 (48.2)		373 (44.5)		461 (51.6)
Psychological distress score, mean (STD)			6	15.3 (11.4)	7	19.0 (12.5)
High psychological distress score[h]	13		6		7	
Yes		381 (22.1)		143 (17.2)		238 (26.7)
No		1342 (77.9)		690 (82.8)		652 (73.3)
Hours worked per week for the organization	24		13		11	
≤40		1601 (93.5)		748 (90.6)		853 (96.3)
> 40		111 (6.5)		78 (9.4)		33 (3.7)
Hours worked per week for another organization	30		10		20	
0		1477 (86.6)		698 (84.2)		779 (88.8)
≥ 1		229 (13.4)		131 (15.8)		98 (11.2)
Employee status, follow-up (2015-2018)	2		1		1	
Yes		507 (29.2)		230 (27.5)		277 (30.9)
No		1222 (70.5)		606 (72.3)		616 (68.8)
Imprecise		5 (0.3)		2 (0.24)		3 (0.33)
Personal history of cardiovascular disease[i]	8		1		7	
Yes		101 (5.8)		54 (6.4)		47 (5.3)
No		1627 (94.2)		784 (93.6)		843 (94.7)
Family history of cardiovascular disease[j]	34		15		19	
Yes		784 (46.1)		356 (43.2)		428 (48.8)
No		897 (52.7)		460 (55.8)		437 (49.8)
Don't know		21 (1.23)		8 (1.0)		13 (1.5)
Gaziano's predicted cardiovascular risk score	53		18		35	
Low				639 (77.8)		814 (94.4)
Moderate or High				182 (22.2)		48 (5.6)

[a] Canadian dollars
[b]Diabetes was measured by the item *"has a doctor ever told you that you have diabetes?"*
[c]Hypercholesterolemia was measured by the item "has a doctor, nurse or other health care professional ever told you that your cholesterol level is too high?"
[d]Hypertension status refer to participants who had high BP or those who reported taking medication to lower their blood pressure.
[e] High waist circumference ≥ 88 cm (in women) or ≥ 102 cm (in men)
[f]10 or more drinks a week in women or 15 or more drinks a week in men
[g] Performed leisure physical activity for 20 to 30 minutes per session at least twice a week
[h] Psychological distress score greater than or equal to the highest quintile (score > 26.19)
[i]Personal history of angina pectoris, unstable angina, acute myocardial infarction, coronary bypass surgery, percutaneous coronary intervention, stroke
[j]A member of the immediate family (father, mother, brother, or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, hemorrhage, thrombosis) under the age of 60 years.

Table 2. Arterial stiffness at follow-up (2015-2018) in men and women according to main cardiovascular diseases risk factors and psychosocial work-related factor at baseline (1999-2001)

	All 1736		Men 839		Women 897	
	N[a]	8.1 (1.7)	N[a]	8.6 (1.9)	N[a]	7.7 (1.4))
Age y						
<55	1602	8.0 (1.5)	750	8.4 (1.7)	852	7.7 (1.3)
≥55	134	9.7 (2.3)	89	10.0 (2.6)	45	9.1 (1.5)
Systolic blood pressure, mmHg						
<140	1625	8.1 (1.6)	750	8.5 (1.8)	875	7.7 (1.4)
≥140	111	9.2 (1.9)	89	9.4 (1.9)	22	8.7 (1.7)
Diastolic blood pressure mmHg						
<90	1567	8.1 (1.7)	717	8.5 (1.9)	850	7.7 (1.4)
≥90	169	8.9 (1.7)	122	9.1 (1.7)	47	8.4 (1.5)
Hypertension status[b]						
Yes	298	8.9 (1.9)	206	9.2 (2.0)	92	8.4 (1.6)
No	1416	8.0 (1.6)	620	8.4 (1.8)	796	7.7 (1.3)
High Pulse pressure[c], (> 60 mmHg)						
Yes	46	9.4 (2.3)	34	9.43 (2.4)	12	9.2 (2.0)
No	1642	8.1 (1.7)	789	8.5 (1.8)	853	7.7 (1.4)
Diabetes[d]						
Yes	34	9.7 (3.0)	16	11.3 (3.5)	18	8.3 (1.6)
No	1702	8.1(1.6)	823	8.5 (1.8)	879	7.7 (1.4)
Hypercholesterolemia[e]						
Yes	493	8.5 (1.8)	320	8.8 (1.9)	173	7.9 (1.4)
No	1242	8.0 (1.6)	518	8.4 (1.8)	724	7.7 (1.4)
High waist circumference[f]						
Yes	229	8.6 (1.8)	124	9.0 (2.1)	105	8.0 (1.3)
No	1457	8.1 (1.7)	715	8.5 (1.8)	792	7.7 (1.4)
Body Mass Index kg/m^2, mean (SD)						
<25	893	7.9 (1.5)	319	8.4 (1.7)	574	7.7 (1.4)
≥25	843	8.4 (1.8)	520	8.7 (1.9)	323	7.9 (1.4)
Daily smoking						
Yes	200	8.3 (1.7)	91	8.7 (1.9)	109	7.9 (1.4)
No	1532	8.1 (1.7)	747	8.5 (1.8)	785	7.7 (1.4)
Physical activity[g]						
Yes	898	8.1 (1.7)	465	8.5 (1.8)	433	7.6 (1.4)
No	834	8.2 (1.7)	373	8.7 (1.9)	461	7.8 (1.4)
Gaziano's predicted cardiovascular risk score						
Low	1453	7.9 (1.5)	639	8.3 (1.6)	814	7.7 (1.3)
Moderate or High	230	9.5 (2.1)	182	9.6 (2.2)	48	9.1 (1.6)
Number of accumulated cardiovascular risk factors						
0-1	1489	8.0 (1.6)	690	8.4 (1.7)	799	7.7 (1.4)
2+	194	9.1 (2.1)	131	9.4 (2.3)	63	8.4 (1.6)
Family history of cardiovascular disease[h]						
Yes	784	8.2 (1.7)	356	8.6 (1.9)	428	7.8 (1.4)
No	897	8.1 (1.6)	460	8.5 (1.8)	437	7.6 (1.3)
Don't know	21	7.7 (1.8)	8	8.4 (2.5)	13	7.3 (1.2)
Job strain						
Low strain	298	8.3 (1.8)	174	8.7 (1.9)	124	7.8 (1.4)
Passive	592	8.1 (1.7)	237	8.6 (1.8)	355	7.7 (1.5)
Active	486	8.2 (1.8)	280	8.4 (2.0)	206	7.8 (1.4)
High strain	344	8.0 (1.4)	141	8.5 (1.6)	203	7.6 (1.2)
Effort-reward imbalance						
Yes	408	8.2 (1.7)	197	8.6 (1.9)	211	7.8 (1.4)
No	1281	8.1 (1.7)	618	8.6 (1.9)	663	7.7 (1.4)

Arterial stiffness (m/s) in different subgroups are presented as mean and standard deviation (SD)
aThe number of observations used
b Hypertension status refer to participants who had high BP or those who reported taking medication to lower their blood pressure.
cPulse pressure = systolic blood pressure – diastolic blood pressure
dDiabetes was measured by the item *"has a doctor ever told you that you have diabetes?"*
eHypercholesterolemia was measured by the item "has a doctor, nurse or other health care professional ever told you that your cholesterol level is too high?"
fHigh waist circumference: ≥ 88 cm (in women) or ≥ 102 cm (in men)
g Performed leisure physical activity for 20 to 30 minutes per session at least twice a week
h A member of the immediate family (father, mother, brother, or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, hemorrhage, thrombosis) under the age of 60 years.

Table 3. Arterial stiffness (m/s) mean differences at follow-up (2015-2018) and 95% confidence intervals according to psychosocial work-related factors at baseline (1999-2001) in men and women

	Modele I	Modele II	Modele III	Modele IV
Job strain in men				
Missing values/785 observations read	6	28	55	79
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	+0.04 (-0.26;+0.33)	+0.11 (-0.19;+0.41)	+0.16 (-0.15;+0.47)	+0.19 (-0.13;+0.51)
Active	-0.11 (-0.51;+0.29)	-0.14 (-0.50;+0.23)	-0.14 (-0.51;+0.23)	-0.05 (-0.42;+0.31)
High job strain	-0.07 (-0.68;+0.53)	+0.04 (-0.50;+0.58)	-0.05 (-0.61;+0.51)	-0.02 (-0.55;+0.50)
Job strain in women				
Missing values /850 observations read	9	44	86	110
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	-0.09 (-0.35;+0.18)	-0.21 (-0.44;+0.02)	-0.20 (-0.42;+0.03)	-0.23 (-0.47;+0.00)
Active	-0.03 (-0.31;+0.24)	-0.06 (-0.31;+0.18)	-0.03 (-0.30;+0.24)	-0.11 (-0.39;+0.16)
High job strain	-0.14 (-0.47;+0.20)	-0.25 (-0.54;+0.03)	-0.20 (-0.53;+0.13)	-0.27 (-0.59;+0.06)
Effort-Reward Imbalance in men				
Missing values /785 observations read	22	44	68	79
ERI (categorical variable)				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.22;+0.47)	+0.02 (-0.27;+0.31)	-0.07 (-0.39;+0.24)	-0.04 (-0.35;+ 0.28)
ERI (continuous variable)	+0.21 (-0.75;+1.17)	-0.06 (-0.89;+0.76)	-0.27 (-1.19;+0.66)	-0.16 (-1.20;+0.89)
Effort-Reward Imbalance in women				
Missing values /850 observations read	21	53	94	110
ERI				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.14;+ 0.39)	+0.05 (-0.16;+0.27)	+0.13 (-0.10;+0.36)	+0.18 (-0.08;+ 0.43)
ERI (continuous form)	+0.17 (-0.36;+0.69)	-0.04 (-0.46;+0.38)	+0.12 (-0.25;+0.49)	+0.18 (-0.28;+0.64)

Model I: unadjusted;
Model II: I+ age, education, income, marital status, children, familial history of cardiovascular disease at baseline.
Model III: II+ systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, body mass index (Kg/m²), waist circumference (cm), lifestyle (alcohol abuse, daily smoking, physical activity), psychological distress score at baseline.
Model IV: III+ hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance) at baseline.
Models are restricted to people with no personal history of cardiovascular disease at baseline.
ERI: effort-reward imbalance

Table 4. Arterial stiffness (m/s) mean differences at follow-up (2015-2018) and 95% confidence intervals according to psychosocial work-related factors at baseline (1999-2001) stratified by blood pressure at the time of exposure

	Systolic Blood pressure, mmHg		Diastolic Blood pressure, mmHg		Pulse pressure, mmHg	
	<140	≥140	<90	≥90	≤60	> 60
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
Job strain						
Low strain	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Passive	-0.02 (-0.23;+0.19)	-0.27 (-1.28;+0.74)	-0.05 (-0.28;+0.18)	+0.03 (-0.72;+0.79)	-0.06 (-0.27;+0.14)	+1.54 (-0.47;+3.55)
Active	-0.05 (-0.28;+0.18)	-0.13 (-1.05;+0.80)	-0.08 (-0.33;+0.16)	+0.43 (-0.18;+1.04)	-0.09 (-0.31;+0.13)	**+2.06 (+0.69;+3.44)**
High job strain	-0.17 (-0.40;+0.07)	+0.84 (-0.35;+2.03)	**-0.25 (-0.48;-0.02)**	**+1.38 (+0.57;+2.19)**	-0.16 (-0.40;+0.08)	**+3.00 (+1.18;+4.76)**
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
ERI						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	+0.13 (-0.08;+0.34)	**-1.17 (-2.12;-0.22)**	+0.11 (-0.12;+0.35)	-0.48 (-1.10;+0.14)	+0.08 (-0.10;+0.27)	**-2.06 (-3.33;-0.79)**
ERI (continuous form)	-0.02 (-0.55;+0.50)	+0.66 (-1.44;+2.77)	-0.04 (-0.57;+0.50)	-0.34 (-1.99;+1.31)	-0.04 (-0.56;+0.48)	+0.43 (-4.69;+5.55)

Models are adjusted for sex and covariates at baseline (age, education, income, marital status, children, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, body mass index (Kg/m^2), waist circumference (cm), alcohol abuse, daily smoking, physical activity, familial history of cardiovascular disease, psychological distress, hours worked per week for the organization, hours worked per week for another organization, ERI (when studying the effect of job strain) or job strain (when studying the effect of ERI).
Models are restricted to people with no personal history of cardiovascular disease at baseline.
Pulse pressure = systolic blood pressure – diastolic blood pressure
ERI: effort-reward imbalance

Figure 1. Flow chart
The start of the original cohort: 1991-1993; Baseline: the baseline for the current study in 1999-2001; Follow-up: the follow-up for the current study in 2015-2018. The current study investigates the association between psychosocial work-related factors measured at baseline (1999-2001) and arterial stiffness measured at follow-up (2015-2018), adjusted for covariates measured at follow-up. Covariates measured at the start of the original cohort (1991-1993) were used to compute inverse probability of censoring weights (used in order to minimize potential selection bias due to non-response and lost to follow-up).

Figure 2. Possible sequences of events between chronic exposure to psychosocial work-related factors and the development of arterial stiffness, hypertension and cardiovascular diseases, based on the cardiovascular continuum
* Adiposity, smoking, alcohol abuse, excessive salt intake, physical inactivity, dyslipidemia, diabetes, mental health, chronic inflammation.

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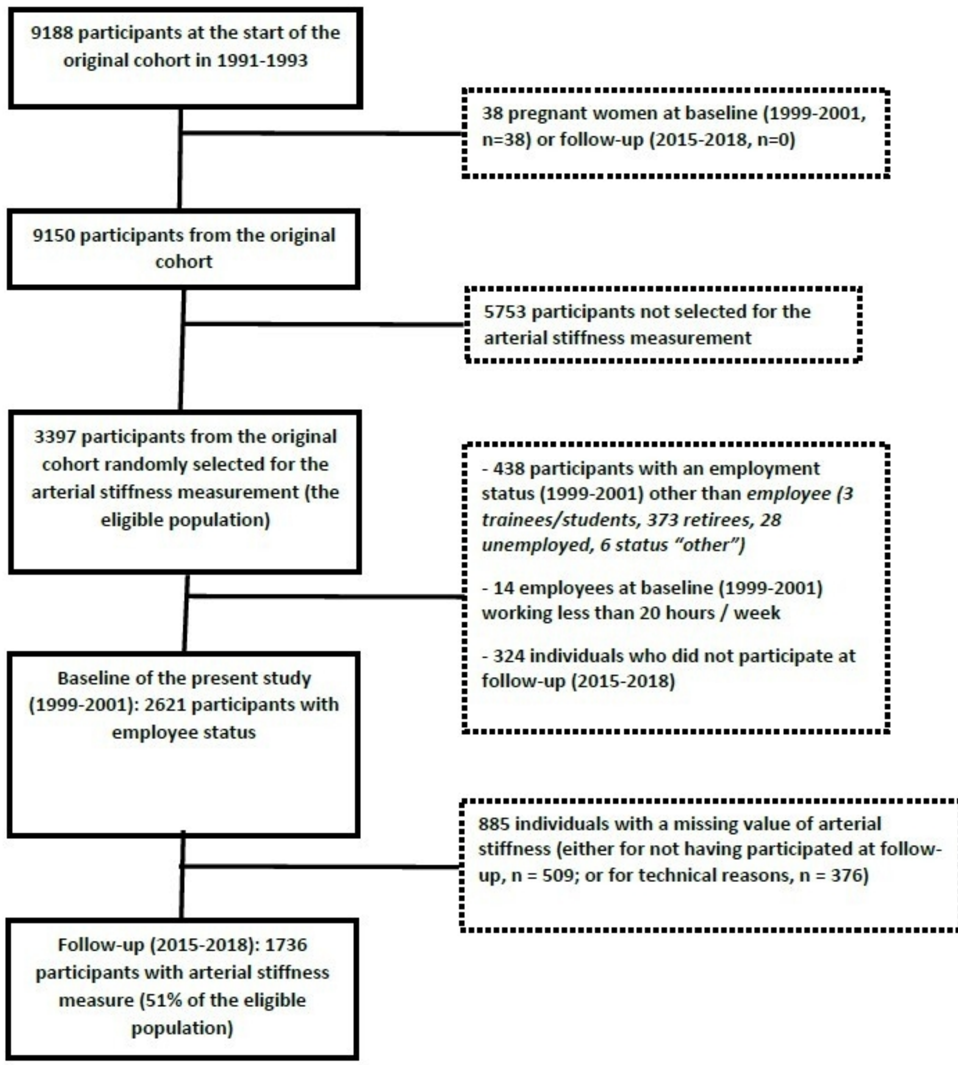

Figure 1. Flow chart
The start of the original cohort: 1991-1993; Baseline: the baseline for the current study in 1999-2001; Follow-up: the follow-up for the current study in 2015-2018. The current study investigates the association between psychosocial work-related factors measured at baseline (1999-2001) and arterial stiffness measured at follow-up (2015-2018), adjusted for covariates measured at follow-up. Covariates measured at the start of the original cohort (1991-1993) were used to compute inverse probability of censoring weights (used in order to minimize potential selection bias due to non-response and lost to follow-up).

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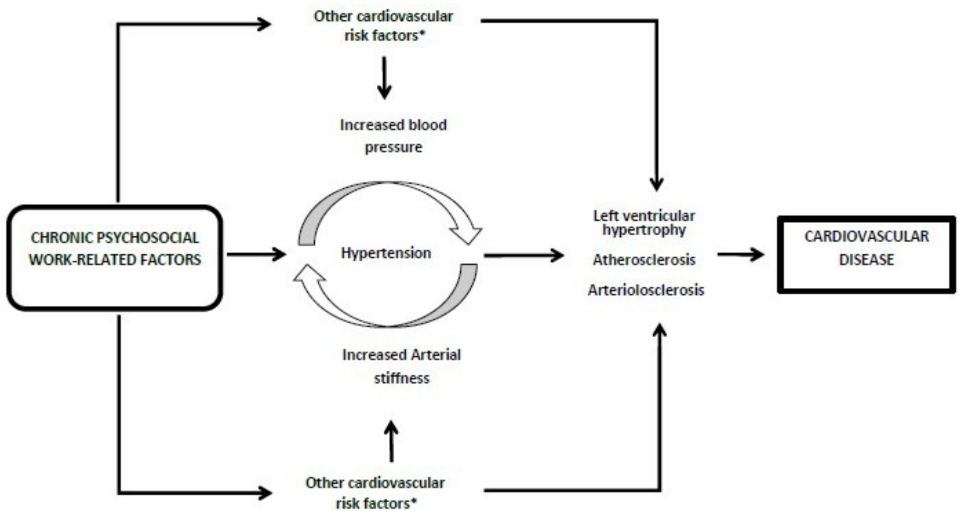

Figure 2. Possible sequences of events between chronic exposure to psychosocial work-related factors and the development of arterial stiffness, hypertension and cardiovascular diseases, based on the cardiovascular continuum
* Adiposity, smoking, alcohol abuse, excessive salt intake, physical inactivity, dyslipidemia, diabetes, mental health, chronic inflammation.

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Table S1. Arterial stiffness (cfPWV in m/s) mean differences at follow-up and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at baseline (1999-2001) stratified by age and Gaziano's predicted cardiovascular risk at the time of exposure

	Age, years		Gaziano's predicted cardiovascular risk	
	<55	≥55	Weak	Moderate or high
Missing/observations read	162/1523	27/112	110/1383	28/201
Job strain				
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	-0.06 (-0.29;+0.17)	+0.25 (-0.74;+1.23)	-0.10 (-0.33;+0.13)	+0.30 (-0.34;+0.94)
Active	-0.07 (-0.31;+0.17)	+0.26 (-0.68;+1.21)	-0.08 (-0.33;+0.17)	+0.16 (-0.40;+0.72)
High job strain	-0.11 (-0.35;+0.14)	+0.55 (-1.23;+2.34)	-0.13 (-0.37;+0.11)	+0.24 (-0.55;+1.03)
Missing/observations read	162/1523	27/112	110/1383	28/201
ERI (2 categories)				
No	Ref.	Ref.	Ref.	Ref.
Yes	+0.06 (-0.13;+0.25)	+0.52 (-0.67;+1.71)	+0.08 (-0.11;+0.28)	-0.20 (-0.77;+0.37)
ERI as a continuous variable	+0.04 (-0.46;+0.54)	-0.32 (-3.25;+2.62)	+0.04 (-0.53;+0.60)	-0.21 (-1.54;+1.12)

Models are adjusted for gender and covariates at baseline(age, education, income, marital status, children, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), diabetes, hypercholesterolemia, BMI, waist circumference (cm), alcohol abuse, daily smoking, physical activity, familial history of cardiovascular disease, psychological distress, hours worked per week for the organization, hours worked per week for another organization, ERI (when studying the effect of job strain) or job strain (when studying the effect of ERI).
Models are restricted to people with no personal history of cardiovascular disease at baseline.
ERI: effort-reward imbalance
cfPWV: carotid-femoral pulse wave velocity
Baseline: 1999-2001; follow-up: 2015-2018

Table S2a. Arterial stiffness (cfPWV in m/s) mean differences at follow-up and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at baseline stratified by employment status at the time of arterial stiffness measurement (fully adjusted model*)

	Employees	Non-employees
Missing/observations read	49/492	139/1137
Job strain		
Low strain	Ref	Ref
Passive	-0.04 (-0.24;+0.16)	-0.05 (-0.28;+0.19)
Active	-0.18 (-0.52;+0.16)	+0.04 (-0.29;+0.36)
High job strain	+0.00 (-0.33;+0.34)	-0.14 (-0.41;+0.13)
Missing/observations read	49/492	139/1137
Effort-reward imbalance (2 categories)		
No	Ref	Ref
Yes	+0.13 (-0.12;+0.37)	+0.05 (-0.23;+0.34)
Effort-reward imbalance as a continuous variable	+0.43 (-0.33;+1.18)	-0.04 (-0.70;+0.61)

*The model is adjusted for covariates at baseline (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).) and for gender
People with personal history of cardiovascular events at baseline are not included.
The category of people with imprecise employment status was excluded from stratification given a low size.
Baseline: 1999-2001; follow-up: 2015-2018

Table S2b. Arterial stiffness (m/s) mean differences at follow-up and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at baseline in participants with the status of retired in follow-up according to the duration of the retirement (fully adjusted model*)

	The duration of the retirement	
	≤ 2 years	> 2 years
Missing/observations read	34/293	90/778
Job strain		
Low strain	Ref.	Ref.
Passive	+0.07 (-0.34;+0.49)	-0.10 (-0.40;+0.19)
Active	-0.14 (-0.54;+0.27)	-0.04 (-0.36;+0.29)
High job strain	-0.24 (-0.69;+0.22)	-0.20 (-0.58;+0.19)
Missing/observations read	34/293	90/778
Effort-reward imbalance (2 categories)		
No	Ref	Ref
Yes	+0.03 (-0.30;+0.35)	+0.20 (-0.14;+0.55)
Effort-reward imbalance as a continuous variable	-0.26 (-0.91;+0.38)	+0.29 (-0.61 ;+1.19)

The model is adjusted for covariates at baseline (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance)) and for gender
People with personal history of cardiovascular events at baseline are not included.
Baseline: 1999-2001; follow-up: 2015-2018

Table S3. Arterial stiffness (m/s) mean differences at follow-up and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at baseline with and without participants with personal history of cardiovascular events* at baseline (fully adjusted models)

Exposure	With individuals with personal history of CVD at baseline (Model A)	Without individuals with personal history of CVD at baseline (Model B)
Job strain in men		
Low strain	Ref.	Ref.
Passive	+0.21 (-0.10;+0.51)	+0.19 (-0.13;+0.51)
Active	-0.11 (-0.45;+0.24)	-0.05 (-0.42;+0.31)
High job strain	-0.02 -0.57;+0.52)	-0.02 (-0.55;+0.50)
Job strain in women		
Low strain	Ref.	Ref.
Passive	-0.18 (-0.40;+0.05)	-0.23 (-0.47;+0.00)
Active	-0.03 (-0.34;+0.28)	-0.11 (-0.39;+0.16)
High job strain	**-0.30 (-0.57;-0.02)**	-0.27 (-0.59;+0.06)
Effort-reward imbalance in men		
No	Ref.	Ref.
Yes	-0.09 (-0.43;+ 0.26)	-0.04 (-0.35;+ 0.28)
Effort-reward imbalance in women		
No	Ref.	Ref.
Yes	+0.22 (-0.10;+ 0.53)	+0.18 (-0.08;+ 0.43)

* Cardiovascular events: angina pectoris, acute myocardial infarction, coronary bypass surgery, dilation
Model A includes covariates at baseline (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, personal history of CVD , psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).).
Model B= Model A without participants with personal history of cardiovascular events at baseline (n=101)
Baseline: 1999-2001; follow-up: 2015-2018

Table S4. Arterial stiffness (m/s) mean differences at follow-up and 95% confidence intervals according to work-related psychosocial factors (job strain and effort-reward imbalance) at baseline before and after correction for selection bias (fully adjusted models*)

	Men			Women		
	No imputation	42 imputations	IPW	No imputations	42 imputations	IPW
Job strain						
Low strain	Ref.	Ref.	Ref..	Ref.	Ref.	Ref.
Passive	+0.19 (-0.13;+0.51)	+0.10 (-0.19;+0.39)	+0.10 (-0.27;+0.47)	*-0.23 (-0.47;+0.00)*	-0.19 (-0.44;+0.06)	-0.12 (-0.49;+0.24)
Active	-0.05 (-0.42;+0.31)	-0.06 (-0.39;+0.28)	+0.01 (-0.43;+0.44)	-0.11 (-0.39;+0.16)	-0.10 (-0.37;+0.16)	-0.08 (-0.49;+0.33)
High job strain	-0.02 (-0.55;+0.50)	-0.07 (-0.50;+0.36)	-0.05 (-0.59;+0.48)	-0.27 (-0.59;+0.06)	-0.25 (-0.59;+0.09)	-0.23 (-0.60;+0.14)
ERI						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	-0.04 (-0.35;+ 0.28)	+0.07 (-0.18;+0.32)	+0.21 (-0.11;+0.55)	+0.18 (-0.08;+ 0.43)	+0.09 (-0.13;+0.31)	+0.07 (-0.22;+0.36)
ERI as a continuous variable	-0.16 (-1.20;+0.89)	+0.25 (-0.64;+1.14)	+0.29 (-0.72;+1.30)	+0.18 (-0.28;+0.64)	+0.13 (-0.43;+0.69)	+0.09 (-0.62;+0.80)

*Models are adjusted for covariates at baseline (age, education, income, marital status, having at least on child, systolic blood pressure, diastolic blood pressure, diabetes, hypercholesterolemia, body mass index, waist circumference, alcohol abuse, daily smoking, physical activity, familial history of CVD, psychological distress, hours worked per week for the organization, hours worked per week for another organization, effort-reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort-reward imbalance).).
Models are restricted to people with no personal history of cardiovascular events at baseline.
ERI: effort-reward imbalance
IPW: inverse probability weighting
Baseline: 1999-2001; follow-up: 2015-2018

References

1. Gaziano TA, Young CR, Fitzmaurice G, Atwood S, Gaziano JM. Laboratory-based versus non-laboratory-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort. Lancet (London, England). 2008;371(9616):923-31.

2. Pandya A, Weinstein MC, Gaziano TA. A comparative assessment of non-laboratory-based versus commonly used laboratory-based cardiovascular disease risk scores in the NHANES III population. PloS one. 2011;6(5):e20416-e.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1;2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4;5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5;6;7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5;6
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8;15;16
		(b) Indicate number of participants with missing data for each variable of interest	15;16
		(c) Summarise follow-up time (eg, average and total amount)	8
Outcome data	15*	Report numbers of outcome events or summary measures over time	8;17

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6;7;18;19
		(*b*) Report category boundaries when continuous variables were categorized	16;17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7;9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10;11;12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13;14

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.